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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/911,904	07/23/2001	Spencer B. Farr	400742000200	4189

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/911,904	FARR ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-49* is/are pending in the application.

4a) Of the above claim(s) *41-44,48 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *703* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed September 22, 2003. Currently, claims 41-49 are pending. Claims 41-44, 48-49 have been withdrawn as drawn to non-elected subject matter.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn.

Election/Restrictions

4. Applicant's election of Group IV in Paper filed February 28, 2003 is acknowledged. The response also elected the single combination of nucleic acids C1-C10, namely SEQ ID NO: 115-124. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 31-40 have been withdrawn as directed to non-elected subject matter since the single combination of genes selected contain 10 genes and are found within Table 2. Claims 24-30 have been examined on their merits.

Newly submitted claims 41-44, 48-49 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons. Claims 41-44, 48-49 are drawn to patentably distinct combinations of nucleic acids on an array, not previously elected or searched. The prior office action requested selection of a single combination of nucleic acids for examination. The response selected SEQ

ID NO: 115-124 without traverse. Therefore, a distinct composition would require further search, consideration and is a patentably distinct invention, for the reasons set forth in the restriction requirement.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 41-44, 48-49 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Priority

5. This application claims priority to provisional application 60/220,057, filed July 21, 2000.

Drawings

6. The drawings are acceptable.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Newly added Claims 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Debouck et al. (Nature Genetics Supplement, Vol. 2, pages 48-50, January 1999) in view of Lillicrap et al. (US Pat. 6,251,632, June 2001) or Aguirre et al (US Pat. 6,201,114, March 2001) and in further view of Pirson et al. (Genbank Accession Number X95367, October 1996) and Yokota (Genbank Accession Number AB008451, October 1997) and Nakamura et al. (Genbank Accession Number AB012918, October 1999) and Van Leeuwen et al. (Genbank Accession Number L37107, February 1997) and Kobayashi et al. (Genbank Accession Number AB028042, November 1999) and Somberg et al. (Genbank Accession Number U28141, June 1995) and Kobayashi et al (Genbank Accession Number D84397, June 1999) and Manning et al. (Genbank Accession Number L31625, April 1994) and Puel et al. (Genbank Accession Number AF045016, February 1998) and Ortiz-Garcia et al. (Genbank Accession Number AF021873, July 1999).

It is noted that the instant specification admits that each of the SEQ ID NO: 115-124 are known in the art, based upon Table 2 (beginning on page 72). However, the

specific Genbank Numbers and alignments have been provided for convenience and completeness.

Debouck et al. (herein referred to as Debouck) teaches the use of DNA microarrays in drug discovery and development to measure expression patterns of thousands of genes in parallel (abstract). Debouck teaches DNA microarrays can be used for both genotyping and measuring mRNA levels to generate information rapidly for the identification and validation of novel therapeutic targets. Debouck teaches numerous benefits of microarrays which include the opportunity to compare the expression of thousands of genes between 'disease' and 'normal' tissues and cells to identify multiple potential targets; studying gene expression in disease models; investigating the mechanism of drug action by measuring the changes in mRNA levels before and after treatment with inhibitors; and monitoring expression of genes with toxicity potential. Debouck suggest that microarrays encompassing at least one element for each expressed gene in a gene organism will soon become available for many organisms (page 50, col. 2).

Debouck does not specifically teach canine expression genes on an array.

However, Lillicrap et al. (herein referred to as Lillicrap) teaches the canine gene for factor VIII. Lillicrap teaches that dogs have been of increasing interest as a canine model system for studying of the physiology of human diseases characterized by factor VIII deficiencies such as hemophilia A. Lillicrap also teaches that the canine has shown promise as a model system for the development of methods of detecting and treating such diseases in humans (col. 4, lines 18-27). Lillicrap teaches methods for detecting

expression of the factor VII gene in canine tissue may be performed by northern blot analysis. Specifically, Lillicrap teaches that bleeding disorders are believed to be due to significantly lower levels of factor VIII gene expression when compared to a "standard" factor VIII gene expression level (col. 20, lines 45-65). Therefore, Lillicrap teaches a method which comprises obtaining a sample of tissue from a canine, assaying for expression in the sample, and comparing the expression level to a standard sample (col. 20, lines 45-65). Therefore, Lillicrap teaches methods of assaying for canine expression levels.

Aguirre et al. (herein referred to as Aguirre) also teaches a canine gene, RPE65, which contains a mutation which affects dogs with congenital stationary night blindness (abstract). Aguirre contemplates assaying for the allele using an array.

Moreover, each gene required by the claims was known in the art at the time the invention was made. Pirson et al. (Genbank Accession Number X95367, October 1996) teaches the c-myc proto-oncogene from canis familiaris, namely SEQ ID NO: 115. The nucleic acids of Pirson and SEQ ID NO: 115 are 100% identical.

Yokota (Genbank Accession Number AB008451, October 1997) teaches the erbB-2 mRNA from canis familiaris, namely SEQ ID NO: 116. The nucleic acids of Yokota and SEQ ID NO: 116 are 100% identical.

Nakamura et al. (Genbank Accession Number AB012918, October 1999) teaches the mRNA for catalase from canis familiaris, namely SEQ ID NO: 117. The nucleic acids of Nakamura and SEQ ID NO: 117 are 100% identical.

Van Leeuwen et al. (Genbank Accession Number L37107, February 1997) teaches the mRNA from p53 from canis familiaris, namely SEQ ID NO: 118. The nucleic acids of Van Leeuwen and SEQ ID NO: 118 are 100% identical.

Kobayashi et al. (Genbank Accession Number AB028042, November 1999) teaches the mRNA from metallothionein isoform 2 (mt-II gene) from canis familiaris, namely SEQ ID NO: 119. The nucleic acids of Kobayashi and SEQ ID NO: 119 are 100% identical.

Somberg et al. (Genbank Accession Number U28141, June 1995) teaches the mRNA from interleukin-2 from canis familiaris, namely SEQ ID NO: 120. The nucleic acids of Somberg and SEQ ID NO: 120 are 100% identical.

Kobayashi et al (Genbank Accession Number D84397, June 1999) teaches the mRNA for metallothionein-1 from canis familiaris, namely SEQ ID NO: 121. The nucleic acids of Kobayashi and SEQ ID NO: 121 are 100% identical.

Manning et al. (Genbank Accession Number L31625, April 1994) teaches mRNA from intercellular adhesion molecule –1 from canis familiaris, namely SEQ ID NO: 122. The nucleic aicds of Manning and SEQ ID NO: 122 are 100% identical.

Puel et al. (Genbank Accession Number AF045016, February 1998) teaches the mRNA from MDR1 from canis familiaris, namely SEQ ID NO: 123. The nucleic acids of Puel and SEQ ID NO: 123 are 100% identical.

Ortiz-Garcia et al. (Genbank Accession Number AF021873, July 1999) teaches mRNA from beta-actin from canis familiaris, namely SEQ ID NO: 124. The nucleic acids of Oritz-Garcia and SEQ ID NO: 124 are 100% identical.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the gene expression array of Debouck to comprises canine genes which were known at the time the invention was made. Debouck teaches that microarrays may be used for both genotyping and gene analysis. The art provides numerous genes from canines which are known to be affected by expression levels and alterations. Therefore, to place canine genes upon arrays to enable simultaneous analysis of a multitude of genes in parallel would have the expected benefit of high throughput analysis. Debouck teaches numerous reasons why analyzing genes on an array is useful. Among these reasons is to study gene expression and toxicological effects of various compounds on gene expressions. The instant claims are drawn to ten canine toxicological response genes which were known at the time of filing. All of these genes are available within the same database, namely Genbank. Placing these well known canine genes, including c-myc, p53, MDR1, beta-actin, upon an array would have been obvious to the ordinary artisan at the time the invention was made. The ordinary artisan would have been motivated to have placed these well known canine genes upon an array to analyze and study the toxicological effects of compounds or environmental effects upon the expression patterns. Moreover, the art clearly suggests that canines may be used a model systems for human diseases. Therefore, placing the instantly claimed genes upon an array would facilitate gene expression of canine nucleic acids which would allow toxicological studies that would be useful for analyzing the model system of the canine which is taught to be of interest for analyzing the human.

Response to Arguments

The response traverses the rejection. The response asserts that there is no suggestion or motivation or teaching in the prior art that would have lead a person of ordinary skill in the art to select the references and combine them in a way that would produce the claimed invention. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, all of the well known genes, as exemplified by the specification and the corresponding Genbank entry, on an array would facilitate gene expression of canine nucleic acids which would allow toxicological studies that would be useful for analyzing the model system of the canine which is taught to be of interest for analyzing the human.

Although the response asserts that "where the prior art does not teach the same utility asserted for the claimed compound, the expectation for the compounds to have similar properties may not arise and the motivation to combine the references would dissipate" (page 12 of response field September 22, 2003). First, it is unclear what applicant's are relying upon to make this blanket statement about the expectation for compounds and their utilities. This statement does not appear to be supported by either facts of record or any established case law. Second, this argument has been

thoroughly reviewed, but is not found persuasive because the arrays suggested by Debouck comprise compounds which are diverse and were "unexpectedly" upregulated (page 49, col 1). Thus, the advantage of profiling the expression of large numbers of genes for studying expression is presented. All of the known canine genes would be useful in gene expression and toxicological effects of various compounds on gene expressions in a high throughput manner. The instant application has not provided any indication or teaches as to why the particular SEQ ID NO: 115-124 is non obvious which would provide any secondary considerations for picking the particular sequences claimed and placing them on an array.

The response asserts that SEQ ID NO: 115-124 were not described to be predictive of toxicity either on their own or in combination with other genes. This argument has been reviewed but is not convincing because the using arrays with known compounds for gene expression and toxicological studies was well established at the time the invention was made. The ordinary artisan, at the time of filing, realized that arrays comprising nucleic acids was a high throughput means of studying many genes simultaneously to determine whether there was any particular effect of various compounds on the expression pattern, whether various genes were expressed in various samples and other properties of nucleic acids.

It is noted that the claims are drawn to a product and the intended use of the product does not carry patentable weight. The canine array containing SEQ ID NO: 115-124 would have additional utilities separate from toxicological screenings. For example, the array may be used to identify a samples as canine, may be used in

paternity screening in canines or may be used in other nucleic acid detection assays. All of the instant sequences would be useful for each of these uses.

Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

9. No claims allowable over the art.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Brandon (US 2002/0187480 A1) teaches that Lion Bioscience recently announced forthcoming release of a dog microarray (para 129).

B) BD Atlas Human cDNA expression array Gene List for cat #7740-1, 1999.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg
Jeanine Goldberg
November 21, 2003

Jehanne Sitton
Primary Examiner
Jehanne Sitton
11/25/03